(FILE 'HOME' ENTERED AT 13:07:10 ON 07 AUG 2003)

FILE 'REGISTRY' ENTERED AT 13:08:12 ON 07 AUG 2003

L1 STRUCTURE UPLOADED

L2 2 S L1 SSS SAM

L3 16 S L1 SSS FULL

FILE 'CAPLUS, MEDLINE, USPATFULL' ENTERED AT 13:10:21 ON 07 AUG 2003

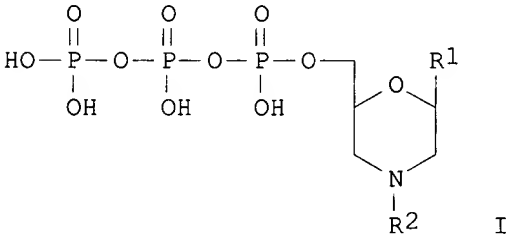
L4 7 S L3

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:608932 CAPLUS
DOCUMENT NUMBER: 133:190215
TITLE: Methods for making morpholino-nucleotides, and their use for analyzing and marking nucleic acid sequences
INVENTOR(S): Marciacq, Florence; Sauvaigo, Sylvie; Mouret, Jean-Francois; Issartel, Jean-Paul; Molko, Didier
PATENT ASSIGNEE(S): Commissariat A L'Energie Atomique, Fr.; Centre National De La Recherche Scientifique
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050626	A1	20000831	WO 2000-FR427	20000221
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2790004	A1	20000825	FR 1999-2170	19990222
FR 2790004	B1	20021129		
FR 2790005	A1	20000825	FR 1999-12001	19990927
EP 1155140	A1	20011121	EP 2000-906441	20000221
EP 1155140	B1	20030528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2003502013	T2	20030121	JP 2000-601189	20000221
AT 241701	E	20030615	AT 2000-906441	20000221

PRIORITY APPLN. INFO.:
FR 1999-2170 A 19990222
FR 1999-12001 A 19990927
WO 2000-FR427 W 20000221

OTHER SOURCE(S): CASREACT 133:190215; MARPAT 133:190215
GI



I

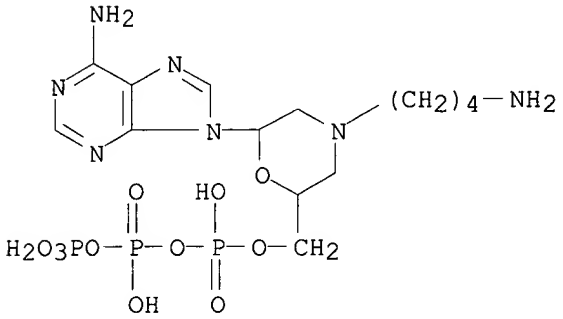
AB The invention concerns the use of morpholino-nucleosides of formula (I) wherein: R1 represents a nucleic base and R2 represents a group corresponding to the following formulas: -(CH2)n-NH2, -(CH2)n-SH, -(CH2)n-COOH, -(CH2)n-OH, -(CH2)n-NH-R3, (CH2)n-SR3-(CH2)n-CO-R3, -(CH2)n-OR3 wherein: n is an integer ranging from 1 to 12 and R3 is a group derived from a marker, a protein, an enzyme, a fatty acid or a peptide, as chain terminators in a DNA or RNA sequencing process by Sanger method, or for marking DNA or RNA fragments.

IT **289639-34-5P**
RL: ARG (Analytical reagent use); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(making morpholino-nucleotides and their use for analyzing and marking

nucleic acid sequences)

RN 289639-34-5 CAPLUS

CN Triphosphoric acid, P-[[4-(4-aminobutyl)-6-(6-amino-9H-purin-9-yl)-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)



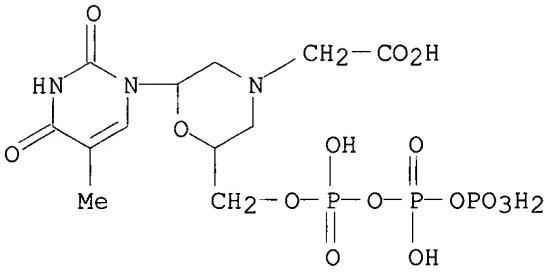
IT **229164-82-3P 289639-39-0P**

RL: ARG (Analytical reagent use); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)

(making morpholino-nucleotides and their use for analyzing and marking nucleic acid sequences)

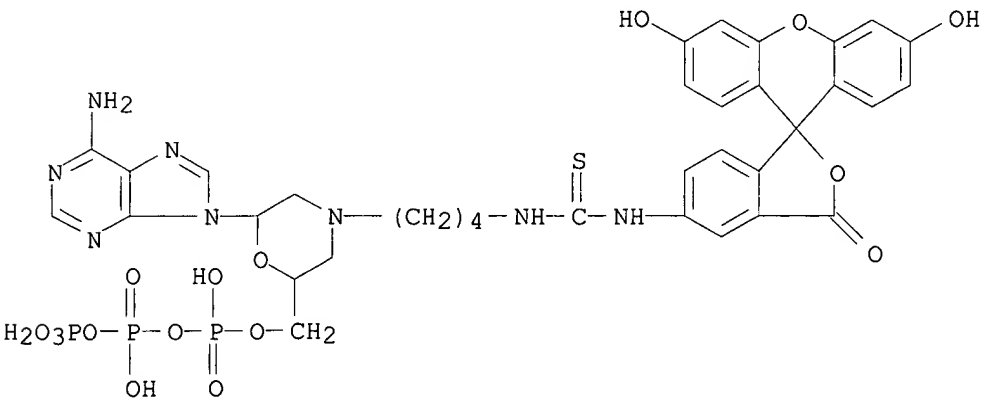
RN 229164-82-3 CAPLUS

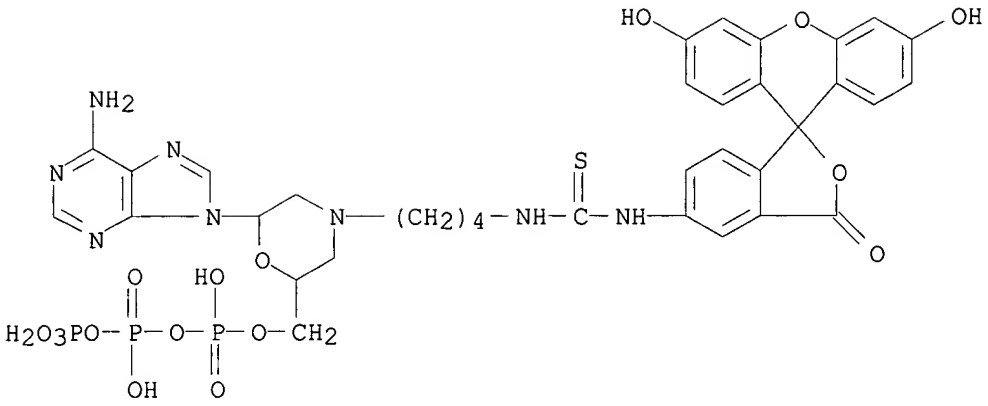
CN 4-Morpholineacetic acid, 2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-6-(3,5,7,7-tetrahydroxy-3,5,7-trioxido-2,4,6-trioxa-3,5,7-triphosphahept-1-yl)- (9CI) (CA INDEX NAME)



RN 289639-39-0 CAPLUS

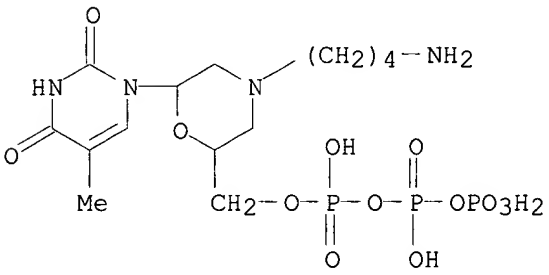
CN Triphosphoric acid, P-[[6-(6-amino-9H-purin-9-yl)-4-[4-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]amino]butyl]-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)



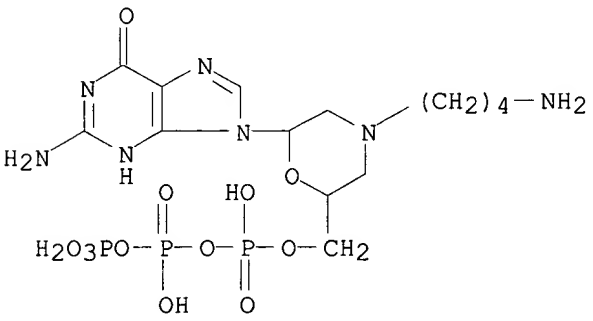


IT **289639-36-7P 289639-37-8P 289639-38-9P**
RL: PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(making morpholino-nucleotides and their use for analyzing and marking nucleic acid sequences)

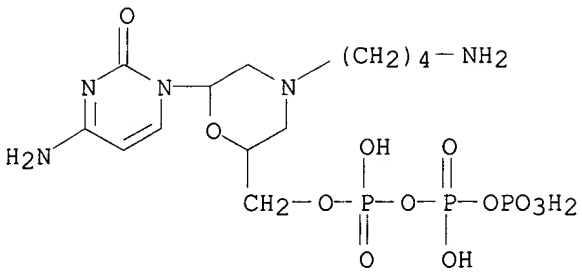
RN 289639-36-7 CAPLUS
CN Triphosphoric acid, P-[[4-(4-aminobutyl)-6-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)



RN 289639-37-8 CAPLUS
CN Triphosphoric acid, P-[[4-(4-aminobutyl)-6-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)

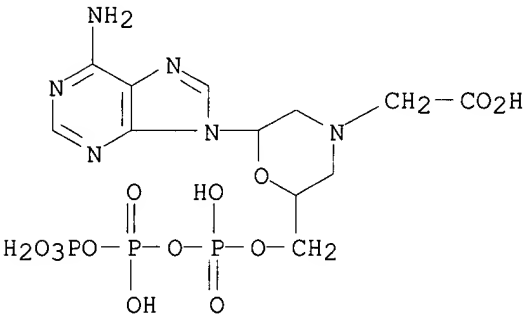


RN 289639-38-9 CAPLUS
CN Triphosphoric acid, P-[[4-(4-aminobutyl)-6-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)

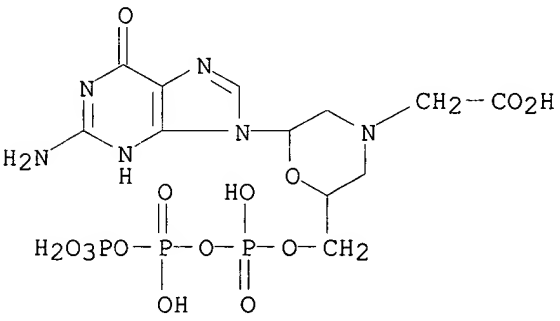


IT **289639-30-1P 289639-32-3P 289639-33-4P**
289639-40-3P 289639-41-4P 289639-42-5P
RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(making morpholino-nucleotides and their use for analyzing and marking nucleic acid sequences)

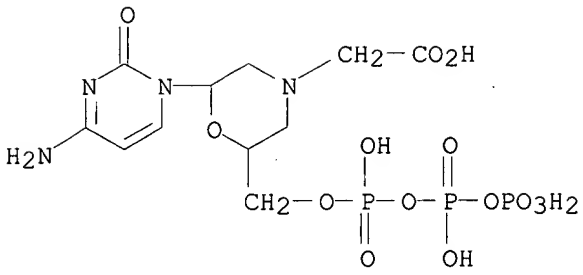
RN 289639-30-1 CAPLUS
CN 4-Morpholineacetic acid, 2-(6-amino-9H-purin-9-yl)-6-(3,5,7,7-tetrahydroxy-3,5,7-trioxido-2,4,6-trioxa-3,5,7-triphosphahept-1-yl)- (9CI) (CA INDEX NAME)



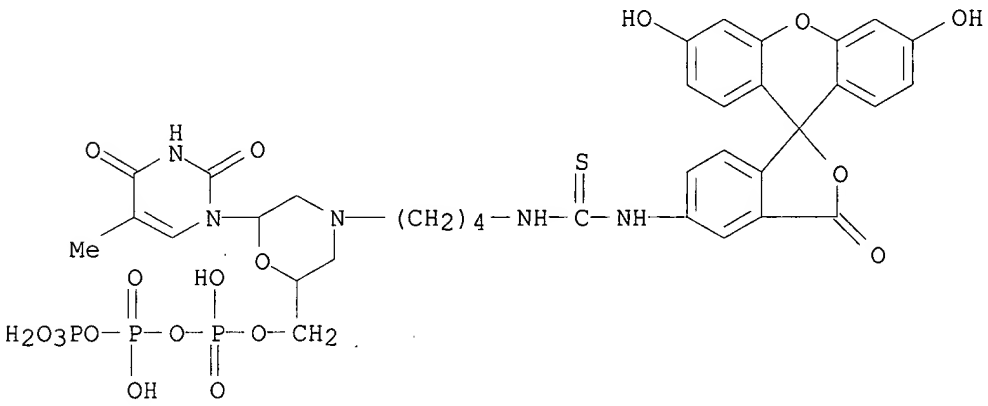
RN 289639-32-3 CAPLUS
CN 4-Morpholineacetic acid, 2-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-6-(3,5,7,7-tetrahydroxy-3,5,7-trioxido-2,4,6-trioxa-3,5,7-triphosphahept-1-yl)- (9CI) (CA INDEX NAME)



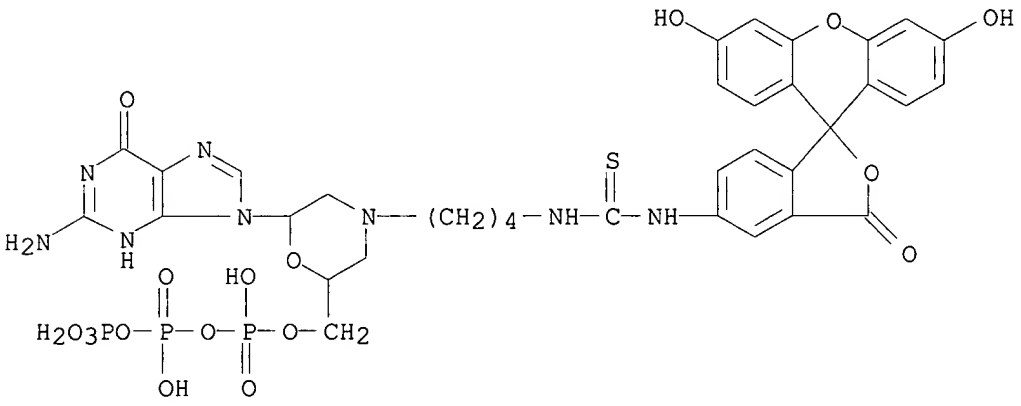
RN 289639-33-4 CAPLUS
CN 4-Morpholineacetic acid, 2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-6-(3,5,7,7-tetrahydroxy-3,5,7-trioxido-2,4,6-trioxa-3,5,7-triphosphahept-1-yl)- (9CI) (CA INDEX NAME)



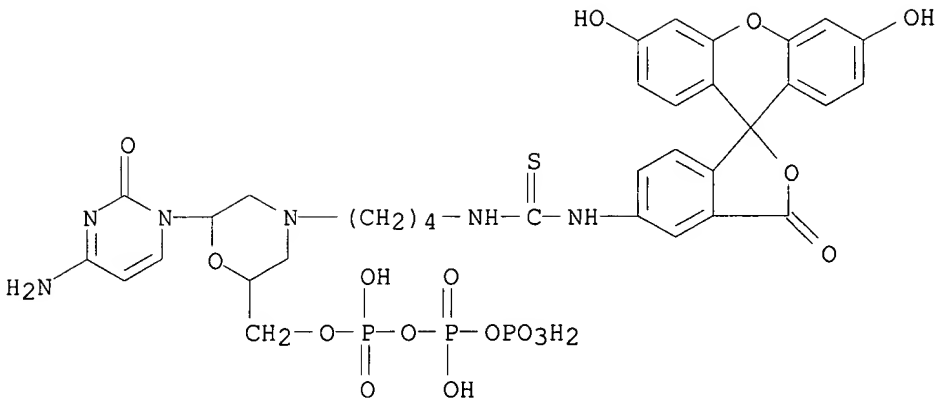
RN 289639-40-3 CAPLUS
CN Triphosphoric acid, P-[[6-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-4-[4-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]amino]butyl]-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)



RN 289639-41-4 CAPLUS
CN Triphosphoric acid, P-[[6-(2-amino-1,6-dihydro-6-oxo-9H-purin-9-yl)-4-[4-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-5-yl)amino]thioxomethyl]amino]butyl]-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)



RN 289639-42-5 CAPLUS
CN Triphosphoric acid, P-[[6-(4-amino-2-oxo-1(2H)-pyrimidinyl)-4-[4-[[[(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthene]-5-yl)amino]thioxomethyl]amino]butyl]-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:122205 CAPLUS
DOCUMENT NUMBER: 132:293960
TITLE: Synthesis, Biological Activity, and Molecular Modeling of Ribose-Modified Deoxyadenosine Bisphosphate Analogues as P2Y1 Receptor Ligands
AUTHOR(S): Nandanan, Erathodiyil; Jang, Soo-Yeon; Moro, Stefano; Kim, Hea Ok; Siddiqui, Maqbool A.; Russ, Pamela; Marquez, Victor E.; Busson, Roger; Herdewijn, Piet; Harden, T. Kendall; Boyer, Jose L.; Jacobson, Kenneth A.
CORPORATE SOURCE: Molecular Recognition Section Laboratory of Bioorganic Chemistry National Institute of Diabetes Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(5), 829-842
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The structure-activity relationships of adenosine-3',5'-bisphosphates as P2Y1 receptor antagonists have been explored, revealing the potency-enhancing effects of the N6-Me group and the ability to substitute the ribose moiety (Nandanan et al. J. Med. Chem. 1999, 42, 1625-1638). The authors have introduced constrained carbocyclic rings (to explore the role of sugar puckering), non-glycosyl bonds to the adenine moiety, and a phosphate group shift. The biol. activity of each analog at P2Y1 receptors was characterized by measuring its capacity to stimulate phospholipase C in turkey erythrocyte membranes (agonist effect) and to inhibit its stimulation elicited by 30 nM 2-methylthioadenosine-5'-diphosphate (antagonist effect). Addn. of the N6-Me group in several cases converted pure agonists to antagonists. A carbocyclic N6-methyl-2'-deoxyadenosine bisphosphate analog was a pure P2Y1 receptor antagonist and equipotent to the ribose analog (MRS 2179). In the series of ring-constrained methanocarba derivs. where a fused cyclopropane moiety constrained the pseudosugar ring of the nucleoside to either a Northern (N) or Southern (S) conformation, as defined in the pseudorotational cycle, the 6-NH2 (N)-analog was a pure agonist of EC50 155 nM and 86-fold more potent than the corresponding (S)-isomer. The 2-chloro-N6-methyl-(N)-methanocarba analog was an antagonist of IC50 51.6 nM; thus, the ribose ring (N)-conformation appeared to be favored in recognition at P2Y1 receptors. A cyclobutyl analog was an antagonist with IC50 of 805 nM, while morpholine ring-contg. analogs were nearly inactive. Anhydrohexitol ring-modified bisphosphate derivs. displayed micromolar potency as

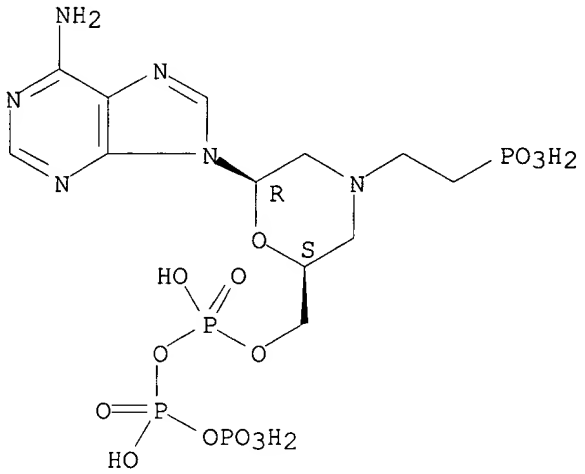
agonists (6-NH2) or antagonists (N6-methyl). A mol. model of the energy-minimized structures of the potent antagonists suggested that the two phosphate groups may occupy common regions. The (N)- and (S)-methanocarba agonist analogs were docked into the putative binding site of the previously reported P2Y1 receptor model.

IT **264611-11-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, biol. activity, and mol. modeling of ribose-modified deoxyadenosine bisphosphate analogs as P2Y1 receptor ligands)

RN 264611-11-2 CAPLUS

CN Triphosphoric acid, P-[[(2S,6R)-6-(6-amino-9H-purin-9-yl)-4-(2-phosphonoethyl)-2-morpholinyl]methyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:380243 CAPLUS

DOCUMENT NUMBER: 131:73915

TITLE: Synthesis and enzymatic incorporation of morpholino thymidine-5'-triphosphate in DNA fragments

AUTHOR(S): Marciacq, Florence; Sauvaigo, Sylvie; Issartel, Jean-Paul; Mouret, Jean-Francois; Molko, Didier

CORPORATE SOURCE: Departement de Recherche Fondamentale sur la Matiere Condensee - Service de Chimie Inorganique and Biologique Laboratoire des Lesions des Acides Nucleiques, Grenoble, 38054, Fr.

SOURCE: Tetrahedron Letters (1999), 40(25), 4673-4676
CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

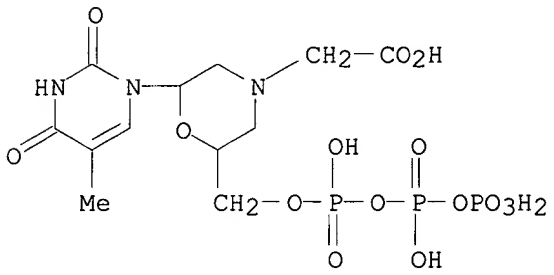
AB 4-(Carboxymethyl)-2-(thymidin-9-yl)-6-(hydroxymethyl)morpholine-6-triphosphate (morpholino thymidine-5'-triphosphate) was synthesized from 1-(.beta.-D-ribo-pentofuranosyl) thymine. It was fully characterized by NMR, UV and mass spectrometry. Taq polymerase enzymic incorporation of this nucleotide analog into DNA fragments was investigated. Morpholino thymidine-5'-triphosphate was incorporated in a base-specific process and acted as a novel chain terminator in DNA sequencing, similarly to the corresponding dideoxynucleotide.

IT **229164-82-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis and enzymic incorporation of morpholino thymidine triphosphate in DNA fragments)

RN 229164-82-3 CAPLUS

CN 4-Morpholineacetic acid, 2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-6-(3,5,7,7-tetrahydroxy-3,5,7-trioxido-2,4,6-trioxa-3,5,7-triphosphahept-1-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1984:22974 CAPLUS

DOCUMENT NUMBER: 100:22974

TITLE: 2,5-Riboadenylate-morpholinoadenylate nucleotides

INVENTOR(S): Torrence, Paul F.; Imai, Jiru; Johnston, Margaret

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: U. S. Pat. Appl., 44 pp. Avail. NTIS Order No. PAT-APPL-6-455 727.
CODEN: XAXXAV

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 468950	A0	19830902	US 1983-468950	19830223
US 4515781	A	19850507		
JP 59205394	A2	19841120	JP 1984-31577	19840223
JP 01053880	B4	19891115		

PRIORITY APPLN. INFO.: US 1983-468950 19830223

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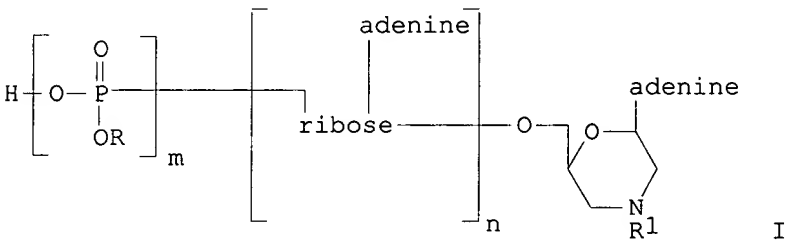


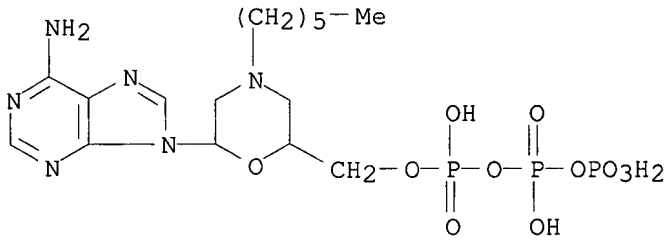
AB The title 2'-5' oligonucleotides I [m = 0-4; n = 1-15; R = H, adenosine, alkyl; R1 = H, (un)substituted hydrocarbyl], useful for fine tuning in antitumoral chemotherapy and for avoiding interferon-induced auto-immune

diseases (biol. data given), were prepd. Thus, 2'-5' (pA)4 was oxidized with NaIO4 and then treated with hexylamine and NaBH3CN to give 85% I (m = 1, n = 3, R = H, R1 = hexyl).

IT **88198-59-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 88198-59-8 CAPLUS

CN Triphosphoric acid, P-[[6-(6-amino-9H-purin-9-yl)-4-hexyl-2-morpholinyl]methyl] ester, sodium salt, (2S-cis)- (9CI) (CA INDEX NAME)



●x Na

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1983:3394 CAPLUS

DOCUMENT NUMBER: 98:3394

TITLE: Chemical modification potentiates the biological activities of 2-5A and its congeners

AUTHOR(S): Imai, Jiro; Johnston, Margaret I.; Torrence, Paul F.

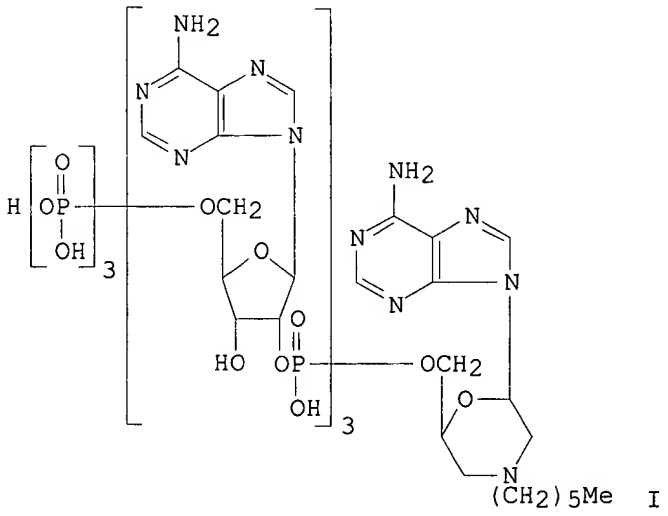
CORPORATE SOURCE: Lab. Chem., Natl. Inst. Arthritis, Diabetes, Dig. Kidney Dis., Bethesda, MD, 20205, USA

SOURCE: Journal of Biological Chemistry (1982), 257(21), 12739-45
CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



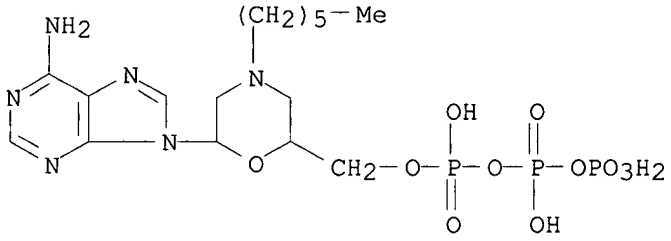
I

AB Chem. modification of p5'A2'(p5'A2')np5'A (oligoadenylates) by a periodate oxidn./Schiff base formation/borohydride redn. cycle gave a series of oligoadenylate analogs in which the ribose of the 2'-terminal nucleotide was transformed to an N-substituted morpholine (azahexapyranose). 2',5'-Oligoriboadenylated 5'-monophosphates bearing this modifications were 5-10-fold more potent as antagonists of the action of ppp5'A2'p5'A2'p5'A2'p5'A (i.e. the unmodified tetramer triphosphate) or poly(I).cntdot.poly(C) than was unmodified p5'A2'p5'A2'p5'A (i.e. the unmodified tetramer monophosphate). Application of this modification to the tetramer triphosphate ppp5'A2'p5'A2'p5'A2'p5'A resulted in an analog (I) with 10-fold the activity of ppp5'A2'p5'A2'p5'A (i.e. the unmodified trimer triphosphate) as an inhibitor of protein synthesis or activator of the 2'.fwdarw.5'-oligoadenylate-dependent endoribonuclease. This new analog, the most potent oligoadenylate deriv. reported to date, inhibited translation in exts. of mouse L-cells programmed with encephalomyocarditis virus RNA at a concn. of 10-10 M (concn. for half-maximal inhibition). All such N-substituted morpholine modified 2'.fwdarw.5'-oligoadenylates were extremely resistant to degrdn. by L-cell exts. under conditions where unmodified 2'.fwdarw.5'-oligoadenylates were quickly destroyed. These data demonstrated the necessity for an intact terminal ribose ring for the action of the 2'.fwdarw.5'-oligoadenylate phosphodiesterase. Thus, extensive chem. modification of the 2' terminus of 2'.fwdarw.5'-oligoadenylate may be possible without adversely affecting its biol. activity while endowing it with other favorable properties such as resistance to degrdn.

IT **83807-25-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 83807-25-4 CAPLUS

CN Triphosphoric acid, P-[[6-(6-amino-9H-purin-9-yl)-4-hexyl-2-morpholinyl]methyl] ester, (2S-cis)- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1979:519380 CAPLUS

DOCUMENT NUMBER: 91:119380

TITLE: Inactivation of phosphofructokinase by dialdehyde-ATP

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LANGUAGE: English

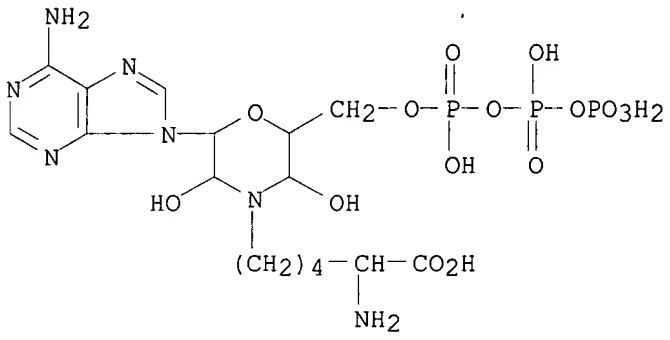
AB Rabbit muscle phosphofructokinase (PFK) was rapidly inactivated by a 2',3'-dialdehyde deriv. of ATP. When allowed to react with 0.6 mM dialdehyde-ATP in 0.1M borate buffer (pH 8.6) contg. 0.2 mM EDTA and 0.5 mM dithiothreitol, PFK lost essentially all activity (99%) in 30 min. The modified PFK remained inactive following dialysis of the reaction mixt. against Na borate (pH 8.0) contg. fructose diphosphate, EDTA, and dithiothreitol. Expts. with 14C-labeled dialdehyde-ATP showed that 99% inactivation of PFK corresponds to incorporation of 3-4 mol of the ATP

analog/PFK protomer. The inactivation of PFK with dialdehyde reagent was not caused by dissocn. of the 340,000 mol. wt. tetramer to the 170,000 mol. wt. dimer, as detd. by anal. ultracentrifugation. ADP or ATP protected PFK from inactivation by dialdehyde-ATP at pH 8.6, but fructose 6-phosphate, cyclic AMP, or fructose diphosphate, which protect PFK from modification by pyridoxal phosphate, provided little protection from inactivation. Amino acid analyses of dialdehyde-inactivated PFK and of a control sample of the enzyme were compared following reaction of each with 2,4-dinitrofluorobenzene. Three or 4 lysine residues/PFK protomer were modified by dialdehyde-ATP. These lysine residues react with dialdehyde-ATP to form dihydroxymorpholine-like adducts rather than Schiff bases.

IT **71316-61-5**
RL: BIOL (Biological study)
(in phosphofructokinase inactivated by dialdehyde-ATP)

RN 71316-61-5 CAPLUS

CN 4-Morpholinehexanoic acid, .alpha.-amino-2-(6-amino-9H-purin-9-yl)-3,5-dihydroxy-6-(3,5,7,7-tetrahydroxy-3,5,7-trioxido-2,4,6-trioxa-3,5,7-triphosphahept-1-yl)-, [2R-[2.alpha.,3.beta.,4(S*),5.beta.,6.alpha.]]-(9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 7 USPATFULL on STN

ACCESSION NUMBER:	85:26900 USPATFULL
TITLE:	2',5'-Riboadenylate-morpholinoadenylate nucleotides
INVENTOR(S):	Torrence, Paul F., Gaithersberg, MD, United States Johnston, Margaret I., Washington, DC, United States Imai, Jiro, Kensington, MD, United States
PATENT ASSIGNEE(S):	The United States of America as represented by the Secretary of the Department of Health and Human Services, Washington, DC, United States (U.S. government)

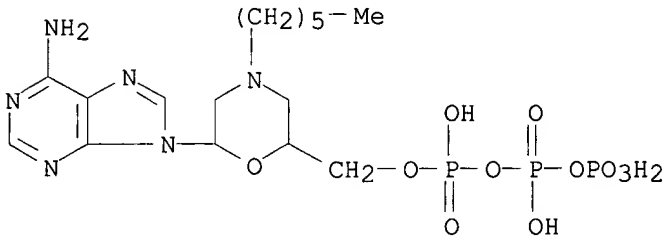
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4515781		19850507	
APPLICATION INFO.:	US 1983-468950		19830223	(6)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Brown, Johnnie R.			
ASSISTANT EXAMINER:	Peselev, Elli			
LEGAL REPRESENTATIVE:	Holman & Stern			
NUMBER OF CLAIMS:	10			
EXEMPLARY CLAIM:	9			
LINE COUNT:	968			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel nucleotide compounds are afforded, having at least one 2',5'-riboadenylate unit and a terminal morpholinoadenylate unit. These compounds have potentiated biological activity in the 2,5-A system and

increased resistance to degradation.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **88198-59-8P**
(prepn. of)
RN 88198-59-8 USPATFULL
CN Triphosphoric acid, P-[[6-(6-amino-9H-purin-9-yl)-4-hexyl-2-morpholinyl]methyl] ester, sodium salt, (2S-cis)- (9CI) (CA INDEX NAME)



●x Na

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